CLINICAL PROCEEDINGS

of the

CHILDREN'S HOSPITAL

WASHINGTON, D. C.

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CLINICAL PROCEEDINGS

OF THE CHILDRENS HOSPITAL

13th and W Streets, Washington 9, D. C.

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CONTENTS

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PNEUMOCOCCAL MENINGITIS

Special Report

Gordon Daisley, M.D.

There have been fifty-six proven cases of meningitis caused by the pneumococcus alone admitted to Children's Hospital between the years 1943 and 1950. These cases have been studied statistically to compare the various elements in them, with particular emphasis on the therapeutic effects and clinical results obtained with the employment of increasing dosages of penicillin in recent years. The fifteen cases of 1943 have been included, although penicillin was not used in a single case, to contrast the therapy before the use of penicillin with the present day regimen.

Pneumococcal meningitis is a disease of infants and young children, slightly more prevalent in males. The disease occurs mainly in the same seasons as does pneumococcal pneumonia; and a history of pneumonia, upper respiratory infection, or otitis media is usually obtainable. Anatomically the spinal meninges usually are only slightly involved, and a heavy exudate of pus and fibrin is sometimes abundant over the anterior lobes of the brain, and less commonly the basilar areas. The diagnosis depends on bacteriologic identification, of course, and usually this is done easily from direct smear. The prognosis is dependent upon the age of the child, the length of time of the existence of the disease, and other concomitant diseases. The spinal fluid cell count is of little value, the number of organisms being more important. This could be seen in our series, in which the counts ranged from 132 to 66,000, but there was no correlation between the counts and eventual outcome[1].

Prior to 1939 and the use of sulfonamides, the recovery of a case of pneumococcal meningitis was rare, and there are two series[2, 3] of over 150 cases each reported in the era in which there were no recoveries. Between the years 1939 and 1946 several reports[4, 5] came out showing that the mortality rate dropped to 60 to 70 per cent with sulfonamides as an adjunct in the therapy. Of the first reports on improvement in results with penicillin, two of the most outstanding were those of Dr. L. K. Sweet et al.[6], in 1945 and Drs. Ross and Burke in 1946[8]. Up through 1948 better and better results were reported, with the mortality ranging from 10 to 20 per cent[7]. A great deal of the literature at this time also dealt with whether or not intrathecal penicillin should be used, and whether or not penicillin given intramuscularly diffused into the cerebrospinal fluid[9, 10]. Since 1948, however, we have been able to find only sporadic case reports on pneumococcal meningitis, and therefore, we thought that this paper might be of some value.

In our series of fifty-six cases, death occurred in twenty-three or 41 per cent. Of the thirty-three patients who lived, twelve were left with residual defects, either permanent or at least not completely cleared at the time of their last follow-up visit to the clinic: this represents a percentage of 21.4 per cent of the total cases, giving an overall mortality and morbidity rate of 62.4 per cent. This has been further broken down into separate years, and is outlined on Figure 1. In 1943, from a total of fifteen cases, ten, or 66.7 per cent died; and three, or 20 per cent, were left with residuals. The year 1944 reveals thirteen cases in total, of which seven or 53.9 per cent died, and three or 23 per cent had residuals. There were seven total cases in 1945; two died and two had residuals, 28.6 per cent in each instance. In 1946 there were two deaths, representing 33.3 per cent, and one case

YEAR	TOTAL CASES	DEATHS		RESIDUALS		MORTALITY AND MORBIDITY RATE
		No.	%	No.	%	
						%
1943	15	10	66.7	3	20.0	86.7
1944	13	7	53.9	3	23.0	76.9
1945	7	2	28.6	2	28.6	57.2
1946	6	2	33.3	1	16.6	50.0
1947	7	2*	28.6	2	28.6	57.2
1948	3	0	0	1	33.3	33.3
1949	5	0	0	0	0	0
Total.....	56	23	41.0	12	21.4	62.4

* One dead on admission.

FIG. 1

with residual, 16.6 per cent, out of six cases. The year 1947 was similar to 1945, but of the two deaths, one was dead on arrival at the hospital. In both 1948 and 1949 there were no deaths in eight cases, and one case with residual in 1948, or 33.3 per cent of that year's total. Looking then at the combined percentages of mortality and morbidity, one can see a continuous improvement over the years, particularly when remembering that one of the deaths in 1947 was dead on arrival. The mortality rate in the last three years also compares favorably or is better than existing reports that we have seen. Of the last eighteen patients treated in this hospital, there has been but one death, and that occurred six hours after admission.*

Also of interest is the apparent decrease in the number of cases for each

* Since compiling this series, there have been two other cases treated successfully and without sequellae.

year after 1944. The incidence would appear to have been cut in half. Quite possibly the early use of chemotherapy and antibiotic in upper respiratory infections and allied diseases has accounted for this.

Thirty-two of the cases, or 57 per cent, were males, and there were twenty-four females. Also, thirty-four were white infants and children; and twenty-two, Negroes. The former figures are consistent with the literature, all large series showing a slight preponderance of males. The latter is about in proportion to the general population in this area. The types of residuals found also correspond roughly with the predominance in the literature. There were five cases of subsequent mental retardation; four cases each of bilateral nerve deafness, hydrocephalus, and spastic quadriplegia; three cases each of subsequent convulsions, blindness, and hemiparesis; two cases of truncal ataxia; and one each of paralysis of the VI

YEAR	AGES OF PATIENTS		
	Average	Oldest	Youngest
1943	0.8 years	5 years	6 days
1944	1.7 years	6 years	7 weeks
1945	2.7 years	14 years	3 months
1946	3.5 years	9 years	6 weeks
1947	0.8 years	3 years	5 weeks
1948	1.2 years	2 years	7 months
1949	1.7 years	4 years	4 months

FIG. 2

and VII cranial nerves. A combination of two or more of these residuals occurred in several cases.

As has been pointed out in the literature, the patient's age, and the duration of symptoms prior to treatment are factors which play a major part in the prognosis; the younger the patient, and the longer he has gone without therapy, the more serious the consequences, naturally. Figure 2 shows the average ages of the patients in the years studied and the span over which they cover. In 1943 the average was 0.8 years, the youngest 6 days, and the oldest 5 years; in 1944, 1.7 years, with 7 weeks to 6 years as the span; in 1945, 2.7 years, running from 3 months to 14 years; in 1946, 3.5 years, from 6 weeks to 9 years; in 1947, 0.8 years, from 5 weeks to 3 years; in 1948, 1.2 years, from 7 months to 2 years; and in 1949, 1.7 years, spanning from 4 months to 4 years. This shows that there has been a rather wide variance in the average ages, but the last three years compare favorably with the first four years, averaging if anything slightly younger, and consequently the prognosis is slightly worse.

Figure 3 shows the average duration of symptoms before admission to the hospital. In order from 1943 they read: 5.1 days, 3.4 days, 5 days, 3.1 days, 2.6 days, 4.7 days and 7.8 days. At first glance this again appears to show that if anything the prognosis was worse for the patients admitted in the last two years, but it must be remembered that over 60 per cent of these cases received some sort of therapy at home, usually chemotherapy or antibiotic. The amounts were not specified in enough instances to be studied, but the doses which were specified were certainly not adequate to prevent the disease, and consequently the extent to which the disease process was modified by this therapy cannot be ascertained.

Early recognition of the meningitis and its type on admission also bears on the prognosis. In all except eleven cases, the diagnosis was made on admission, and the organism was identified within twenty-four hours. In the vast majority the pneumococci were seen on direct smear, and within

YEAR	AVERAGE DURATION OF SYMPTOMS PRIOR TO ADMISSION
	days
1943	5.1
1944	3.4
1945	5.0
1946	3.1
1947	2.6
1948	4.7*
1949	7.8*

* Over 60 per cent received therapy at home.

FIG. 3

four hours after admission, the full diagnosis was known. Six of the eleven cases, which went unrecognized from one and one-half to six days, were in 1943 and 1944; five of these died. Only one, however, did not receive chemotherapy in dosages usually used at that time for the disease. The sixth case received antibiotics also from admission, and recovered fully. The remainder of the cases, one in each year from 1945 to 1950, went unrecognized for from two to four days, but all received large doses of penicillin and sulfa, and all recovered without sequellae.

After seeing these figures, I think we are justified in saying that the ages of the children in the series, and the duration of time before active therapy was instituted are not the significant factors in the better results obtained in the last three years. And, therefore, the improvement should be considered to be due in large to the differences in therapy used.

In addition to better mortality and morbidity rates, the average hospital

stay, and the duration of fever and time for clinical improvement have been shortened, as can be demonstrated from the next figures. Unfortunately, accurate statistics as to the clearing of the organism from the cerebrospinal fluid were not obtainable from the charts, since lumbar punctures in the later years were not done as repeatedly as before, but it is our impression that this time, too, probably is shortening, since practically all of the second lumbar punctures were sterile in the last two years, whereas often in the past, the fluids remained positive for organisms, or returned to positive, two or even three weeks after hospitalization was begun. No conclusions could be drawn, however.

Figure 4 illustrates the average hospital stay for the various years. In 1943 the total hospitalization was 480 days, an average of 32 days. Total days in 1944 were 351, averaging 27 days; in 1945, 186 days, averaging 26.5 days. In 1946 the average was 13 days, from a total of 78. In 1947

YEAR	DURATION OF HOSPITAL STAY		
	Total time	Average	Revised
	days	*days*	*days*
1943	480	32	55
1944	351	27	40
1945	196	26.5	37
1946	78	13	20
1947	113	16	23
1948	44	15	15
1949	103	21	21

FIG. 4

there was a total of 113 days with an average of 16 days; in 1948 the total was 44 days with 15 days average; and in 1949 there was a total of 103 days with a 21 day average. You will note that there is a second column of figures (revised) and we believe that this represents a truer picture of the average hospital stay. Because death occurred rapidly in most instances throughout the years when it occurred, we recalculated the averages, leaving out the cases which were in the hospital less than six days. This eliminated all but three of the deaths, and gives a better picture of how long it took to cure the disease when it was able to be cured. Thus, in 1943 eight cases were discarded which accounted for 24.5 days (this averages three days a case and perhaps should have been retained). However, in 1944 five cases were left out which accounted for only 6.75 days. There were two cases in 1945—a total of 12 hours, two in 1946—a total of 36 hours, and two in 1947—a total of six hours. The revised figures then read in order: 55 days, 40 days, 37 days, 20 days, 23 days, 15 days, and 21 days.

It would seem from the figures that hospitalization for pneumococcal meningitis has been stabilized at about three weeks since 1946. It may be, however, that two weeks will be the figure, as in 1948, since one case alone in 1949 required 37 days hospitalization. This was a two and one-half year old colored boy who had had symptoms ten days prior to admission without any therapy at all; had 15,000 cells in his initial spinal fluid tap, and was moribund on admission. Another case of 1949 had his stay prolonged because he developed chicken-pox on the ward.

The duration of fever in these cases was also studied, since it seemed the best criterion for determining the speed with which the active processes of the disease were overcome. Clearing in the cerebrospinal fluid of the organisms would have been more accurate, of course, but as has been stated before, these times were not obtainable from the charts. Figure 5 outlines the average days of fever, and again there is a second column in which

YEAR	AVERAGE DURATION OF FEVER IN THE HOSPITAL	
	Actual	Revised
	days	*days*
1943	7.7	16
1944	7.3	12
1945	10.0	14
1946	4.7	7
1947	4.0	5.5
1948	4.7	4.7
1949	5.4	3.4

FIG. 5

the averages were revised in the same way as before, deleting the same cases. The actual figures are: 1943, 7.7 days; 1944, 7.3 days; 1945, 10 days; 1946, 4.7 days; 1947, 4 days; 1948, 4.7 days; and 1949, 3.4 days. The recalculated values are 16 days, 12 days, 14 days, 7 days, 5.5 days, 4.7 days, and 3.4 days. These figures seem significant to us, and the rapidity with which the disease is being controlled now may account for the paucity of residuals seen, since the formation of pus and exudate over the brain may be prevented. In any event, the increasing effectiveness of the therapy seems very evident.

Therapy in 1943 consisted of sulfathiazole, sulfadiazine, type-specific antisera against the pneumococcus, and transfusions. Two patients received no therapy. The drug of choice seemed to be sulfadiazine, being used in twelve instances, nine of which averaged between 2 and 3 grains per pound per day. The other three received approximately 2 grains per pound per day. The sulfa was given by clysis usually, and blood levels were checked daily in most instances, with levels from 12 to 20 milligrams per 100 cubic centi-

meters considered as optimal. In the patients who lived, the drug was used for at least two to three weeks, and in two cases for two months. Eight patients received type-specific antiserum, varying from 150,000 to 300,000 units, and four of the five patients who lived received it. Five patients received transfusions, from two to eight each; four of these lived. The most effective therapy was a combination of the three agents; three of the five patients receiving them.

In 1944 penicillin, both intramuscular and intrathecal, was added to the list of therapeutic agents. Of the thirteen cases, eight received intramuscular penicillin; and five, intrathecal. Two cases again received no therapy. Ten of the patients received sulfadiazine; six, antiserum; and five, transfusions. The dosages of sulfa and antiserum remained exactly as before, and one of the six who lived received these alone. The remaining five received 10,000 units of aqueous penicillin every three hours for from nine to twelve days, and the total dosage of penicillin ranged from 720,000 to 960,000 units. Three patients who received the same doses did not survive. Two of the living patients received intrathecal pneicillin, from 5,000 to 10,000 units at a time, four and nine times respectively; three who received this failed to survive. Two of the six surviving received antiserum; all got sulfadiazine. Transfusions were given to four who lived, from six to fourteen transfusions each. As can be seen there was no standard method of therapy, and there were scarcely two consecutive cases treated alike in this year. A combination of sulfa, penicillin, and transfusions was effective in four cases.

In 1945 one patient died without receiving any therapy, and one died after single doses of penicillin and sulfadiazine had been given. The remaining all received the same therapy. Sulfadiazine was given as before, 2 to 3 grains per pound per day, and on the average of seventeen days. The intramuscular dose of penicillin varied from patient to patient, and from day to day in the same patient, as it has done in each succeeding year, but the majority of cases are very similar. The smallest dose given in 1945 was 10,000 units every three hours; and the largest, 30,000 units every two hours. Average dosage was approximately 120,000 units per day, and the average course of therapy was twenty-three days. The total dosages varied from 840,000 units to 6,605,000 units. Intrathecal penicillin, 5,000 units, was given to each, on the average, seventeen times (one case, however, received forty injections). Supportive transfusions were given to four patients (from one to four transfusions each). Of the two patients with residuals, one received 840,000 units of penicillin in seven days, sulfa for six days, and three intrathecal injections. The other patient received 5,290,000 units in fifty-four days, sulfa for thirty days, and forty intrathecal injections.

Therapy was also fairly standard in 1946, and the same agents were employed. Both patients who died had been started on therapy of 30,000 units of penicillin every three hours and received sulfa and intrathecal penicillin. The four surviving cases received sulfadiazine on the average of sixteen days, with blood levels averaging from 7 to 15 milligrams per 100 cubic centimeters; this figure is slightly lower than before. Intramuscular penicillin dosage varied as before, but averaged about 240,000 units per day. The lowest dose used was 20,000 units every three hours (160,000 units per day), and the highest was 100,000 units every two hours (1,200,000 units per day). Total dosage varied from 1,760,000 to 17,180,000 units, but all save one were under 3,000,000 units. The duration of this therapy averaged seventeen days. Intrathecal penicillin was given to two of these four patients, 5,000 units at a time, two and six times respectively. The one case with residual was treated for thirty-five days, receiving 17,180,000 units of penicillin, sulfa for thirty days, and six intrathecal injections. The initial dose was 30,000 units every two hours in this case, a two month old infant. Supportive transfusions were again given in two cases.

The average dose of penicillin per day in 1947 was 400,000 units, and it was given on the average of fourteen days. Sulfa was given on the average of fourteen days also, except in one instance when it was only given for two days because of genito-urinary complications. Intrathecal penicillin was given to three patients, two, three, and five injections each. The total dosage of penicillin ranged from 2,400,000 units to 8,900,000 units; the lowest dose used was 20,000 units every two hours (240,000 units per day) and the highest was 200,000 units every three hours. No transfusions had to be given.

In 1948 the average number of days for both sulfa and penicillin therapy dropped to ten days each. The blood sulfa level averaged 8 milligrams per 100 cubic centimeters, but one case was carried at 2 to 4 milligrams per 100 cubic centimeters. This patient received 200,000 units of penicillin every two hours as his initial dosage, and received 12,400,000 units in toto over a ten day period. Another patient received 100,000 units every three hours initially, and totaled 8,000,000 units in twelve days. He also received three intrathecal doses of penicillin. The last case was carried on sulfa and 300,000 units of penicillin twice daily. His total dose was 5,400,000 units in nine days. The average dose of intramuscular penicillin in these cases was thus 860,000 units per day.

In 1949 the average patient was treated for fourteen days with both penicillin and sulfadiazine in spite of the fact that all but one appeared clinically well in four days' time. As in the preceding year, the blood sulfa level aimed at between 7 and 15 milligrams per 100 cubic centimeters, but the average dosage of penicillin was 4,000,000 units a day initially, or

500,000 units every three hours.* One patient received 1,600,000 units a day initially; and another, 8,000,000 per day. The total doses ranged from 22,800,000 units over a fifteen day period to 217,000,000 units over a nineteen day period. Two patients received intrathecal doses of penicillin, two and four doses respectively. Of two patients of the five receiving sulfa, one received it for only thirty-six hours, and another never had a blood level over 3 milligrams per 100 cubic centimeters.

A summary of the therapy used from 1943 to 1950 is outlined on Figure 6, and shows the increasing dosages of penicillin; the slightly decreasing dosage of sulfadiazine; a trend away from intrathecal medication; a decrease in the average number of days needed for therapy; and for all intents and purposes, the discarding of transfusions and type-specific antisera as active treatment of the disease.

YEAR	SUMMARY OF THERAPY					
	Penicillin		Sulfa average no. days	Total no. intrathecal penicillin injections	Total transfusions	Total u. antiserum
	Average dose per day	Average no. days				
1943	0	0	21	0	20	1,725,000
1944	80,000	10.5	21	19	41	1,500,000
1945	120,000	23	17	76	9	0
1946	240,000	17	16	13	5	0
1947	400,000	14	14	10	0	0
1948	860,000	10	10	3	0	0
1949	4,000,000	14	14	6	2	0

FIG. 6

In summary, fifty-six cases of pneumococcal meningitis have been reviewed and the mortality and morbidity rates; the age, sex, and color; the duration of symptoms prior to therapy; fever; the average hospital stay; and the different therapy employed have been tabulated.

CONCLUSIONS

1. The mortality and morbidity rates of pneumococcal meningitis have decreased markedly since 1943.
2. The average length of time for hospitalization has decreased.
3. The average duration of fever, which was the best criterion of the active disease process in this series, has decreased.
4. The average ages of the patients contracting pneumococcal meningitis

* Since completion of this paper, the average daily dosage has now reached 12,000,000 units per day.

and the duration of symptoms prior to the institution of active therapy have not changed materially since 1943.

5. The increased effectiveness in the control of pneumococcal meningitis is probably due to the increased dosage of penicillin used.

6. We believe this paper serves to point out that further work should be done to determine whether or not sulfadiazine is now necessary in the treatment of this disease, and whether or not the large, intramuscular dosages of penicillin may not make intrathecal doses unnecessary.

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FATAL KEROSENE INTOXICATION

Case Report No. 193

Martin H. Smith, M.D.

J. O., a fifteen month old colored boy, was admitted to Children's Hospital on an evening in July and died three hours later. The child had been in good health until one hour before admission when he was found gasping, choking, and coughing, and holding an empty kerosene can. Shortly afterward, he vomited several times, became cyanotic and semi-stuporous, and was rushed to the hospital.

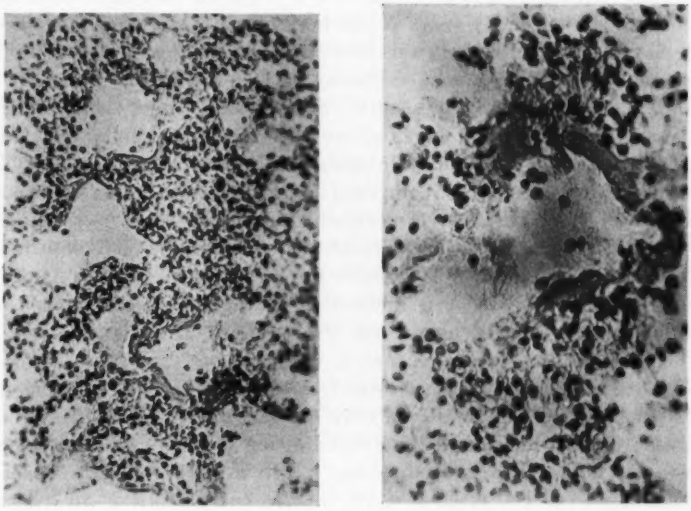
On arrival, the patient was cold, cyanotic, and unresponsive. There was an odor of kerosene on his breath and his respirations were rapid and labored. Coarse rhonchi were heard initially in all lung fields and one hour later medium, moist, crepitant

rales could also be discerned. The heart sounds were rapid and thready; the rate, 180 per minute.

The child's stomach was promptly lavaged and he was placed in an oxygen tent. Penicillin and fluids were given parenterally. He failed to respond to these measures, became more cyanotic and dyspneic, and died, apparently in congestive heart failure.

PATHOLOGIC DISCUSSION

Richard J. Waters, M.D.: A post-mortem examination was performed by the Deputy Coroner and witnessed by us. The significant gross and microscopic findings were as follows:



A B

FIG. 1

A. Low Power
B. High Power
Histologic section of lungs showing hyaline-like membranes lining alveoli.

Both pleural spaces were filled with approximately 150 milliliters of clear, yellow fluid. The lungs were large, firm and dark red. The cut surfaces bulged, bled freely, and released no air from the alveoli. The liver was enlarged, extending 5 centimenters below the right costal margin. The other organs appeared normal in situ.

Histologically, the pleura was widened, edematous, and contained many mononuclear cells. The alveolar walls were thickened and infiltrated with numerous mononuclear (some pigment-laden) macrophages.

The bronchi and the alveoli contained a deeply eosinophilic precipitated

protein substance (representing edema and fibrin) and pigment-bearing macrophages. Many alveoli were lined with thin membranes of an eosinophilic hyaline-like material. (Figure 1). Sections of the thymus, spleen, liver, pancreas, and kidneys were not abnormal.

The pathological diagnosis was as follows:

1. Bilateral diffuse pneumonitis (chemical)
2. Pulmonary edema
3. Pleural effusion.

DISCUSSION

Adrian Recinos, Jr., M.D.: This case is reported because it represents the first fatality in many years at this hospital from ingestion of kerosene. A recent review[1] of our records revealed that kerosene was by far the most frequent offender among the many poisons ingested by our patients, accounting for 54 of 250 consecutive cases studied. There were no deaths in these 54, nor were there any fatalities in 20 more which followed. Hence, there has been only 1 death in 75 cases, a mortality of 1.3 per cent. This is a commendable figure when compared with the overall average of five other series[2, 3, 4, 5, 6], 4.5 per cent (13 deaths in 286 cases).

It is of interest to note that although many fatal cases have occurred in infants and children, many of whom have swallowed small amounts of kerosene, adults are peculiarly immune to death even after ingesting considerable quantities. Deichman[7] in 1944, reported that there were no kerosene fatalities in adults on record.

Kerosene intoxication occurs most frequently as a result of accidental ingestion by infants and children from ten months to three years of age. Kerosene is used for illuminating and heating purposes in lower-income households. Its careless use and storage results in not infrequent poisoning of small children. Too often is it left in coca cola bottles or milk glasses within easy reach of exploring youngsters who become innocent victims.

The pathogenesis of kerosene intoxication, particularly in regard to the pulmonary changes, has stimulated considerable study. Kerosene damages tissues as a result of its irritant action. An acute exudative inflammatory reaction and corrosive lesions occur on the skin or the mucus membranes of the mouth, respiratory or gastroenteric tracts. The severity of the lesions and the degree of healing depend on the concentration of kerosene and the duration of its contact with the tissues.

The ingested kerosene is rapidly absorbed from the gastrointestinal tract and travels to all the organs by way of the blood stream. A generalized toxemia ensues with central nervous system depression and variable changes in the lungs, liver, kidney, and heart. Vascular damage consisting of cloudy swelling and perivascular extravasation of fluid and collections of mono-

nuclear cells constitute the basic lesion in all the organs. Degeneration and necrosis may occur in the heart, liver, and kidney.

The pulmonary lesions are most important and are usually responsible for the fatal cases. Immediately after swallowing kerosene the patient invariably vomits, gags, coughs, and chokes. There is little doubt that some aspiration of the poison takes place initially with irritation of the bronchi, bronchioles, and alveoli. In addition, absorbed kerosene is carried to the lungs and damages them producing hemorrhagic stasis, edema, fibrin, and a diffuse lobular pneumonitis. Because of its low volatility the kerosene is not readily passed from the lungs in the expired air, but instead is retained as a continuing injurious agent. Deichman and his associates[7], unlike earlier observers[8], are convinced that it is the *absorbed* rather than the *aspirated* kerosene which does the bulk of the damage, and feel that every effort should be made to remove the kerosene from the gastrointestinal tract.

Our little patient was typical of the fatal cases. He was a victim of the carelessness of an adult who left a can of kerosene within his reach. A lethal amount of this substance was aspirated and absorbed into his lungs producing severe corrosive lesions and an inflammatory exudate consisting of edema, fibrin (some of which typically was plastered against the alveolar lining), and a mononuclear cellular reaction. Death came rapidly, as is usual in fatal cases, as congestion and consolidation replaced the respiratory tissue.

The treatment, although prompt and thorough, proved ineffective. Little can be done to forestall a fatal outcome in such quickly fulminating cases.

The following measures should be instituted in the management of patients who have ingested kerosene:

1. Dilute and remove the poison by immediate and continued gastric lavage, using large amounts of water or dilute baking soda solution.
2. Reduce its absorption by saline cathartics and high colonic enemas or colon irrigations.
3. Combat shock, maintain circulation and respirations, and minimize pulmonary edema by employing heat, oxygen, stimulants, hypertonic solutions, other fluids including blood.
4. Prevent pneumonia by prophylactic chemo or antibiotic therapy.

SUMMARY

A typical case of fatal kerosene poisoning in a fifteen month old child is presented. The gross and microscopic pathologic findings are reviewed.

The futility of treatment in this type of case is emphasized and a plea for prevention is made.

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LEUKEMOID REACTION

Case Report No. 194

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Muriel Sowers, M.D.
William A. Howard, M.D.

The response of the bone marrow to various irritants can often cause confusion in the minds of clinicians and pathologists. A leukemoid reaction is one example of such an instance.

A leukemoid reaction consists of[1]:

1. A total white blood cell count over 50,000 per cubic millimeter;
2. The presence of immature cells of the "blast" stage; or
3. A combination of both 1. and 2.

A further possibility is a white count which is less than 50,000 and where there is a marked predominance of one type of cell which is not of the "blast" type.

A leukemoid reaction must be chiefly differentiated from leukocytosis and from leukemia. Leukocytosis refers to a total leukocyte count above 10,000 to 11,000 per cubic millimeter, but below 50,000 per cubic millimeter. The laboratory differentiation between a leukemoid reaction and leukemia can be given in tabular form.

A further differentiating point is that in leukemoid states the hematologic response is secondary to other causes while leukemia is a primary condition.

These above-mentioned causes can be divided into four major groups[2].

These are as follows: (1) infection; (2) intoxication; (3) malignancy; and (4) hemorrhage.

Infection: Pneumonia, meningococcus meningitis, and diphtheria produce a neutrophilic myelocytic response. Parasitism[3, 4], tuberculosis, and coccidiomycosis[5] with pulmonary involvement may cause an eosinophilic state. Pertussis[6], varicella, and infectious mononucleosis show a lymphocytic reaction.

Intoxications: Rare instances in eclampsia (100,000 leukocytes per cubic millimeter) and following severe burns (80,000 per cubic millimeter) have been described.

Malignancy: Leukemoid pictures in association with and without bone metastasis have been reported. Hodgkin's disease[6] prominently causes a leukemoid reaction in which eosinophiles are occasionally the only proliferating cell.

TABLE I

Leukemoid Reaction	*Leukemia*
1. Immature as well as mature leukocytes show normal morphology.	1. Leukocytes are atypical particularly the immature ones.
2. Blast forms may be present but usually are under 10 per cent.	2. Blast forms may be numerous, as high as 99 per cent.
3. Immature red cells (normoblasts and erythroblasts) often increased in proportion to leukocyte immaturity.	3. Immature cells rarely increased in proportion to leukocyte immaturity.
4. Platelets usually normal or increased but may be moderately decreased.	4. Platelets decreased, often severely; may be increased in chronic myelogenous form only.
5. Anemia varies depending on causal factor.	5. Steadily progressing anemia becoming extreme.

Hemorrhage: Severe hemorrhage and sudden hemolysis of blood as in familial hemolytic jaundice may cause a myelocytic response.

The clinical picture in a leukemoid state is that of the primary disease, but in addition; fever, hemorrhage, hepato-splenomegaly, and adenopathy may frequently be found[2, 4].

Case Report C. S. 50-8104

C. S., a two month old colored male, was admitted to this hospital on July 3, 1950 with the chief complaint of a "cold" of one week's duration. This was followed by a cough and cyanotic spells during the evening of admission. Just before admission the patient was noted to have loose, brownish-green stools.

The birth weight was 7 pounds, 2 ounces. The patient had been on an evaporated milk formula and since birth had vomited one-half ounce of his feeding shortly after taking it. At one month of age, a rash appeared over his body and he was taken to a clinic where a diagnosis of "allergy" was made. The formula was changed to homogenized milk. The family history was negative for tuberculosis, syphilis, and blood disease.

The physical examination revealed a poorly developed and poorly nourished colored male infant who appeared acutely and chronically ill. The temperature was 102.4 F. and he weighed 8 pounds. There was a dry, scaly eruption over the entire body more marked on the face. There were also several, scattered, umbilicated lesions on the trunk and extremities. All the lymph nodes were enlarged, firm and discrete. The respirations were rapid and deep, with an inspiratory crow and paroxysmal cough ending in a slight whoop. The lungs showed dullness to percussion in the right upper chest posteriorly with diminished breath sounds in the same area. The liver was 3 centimeters below the right costal margin and was firm and smooth. The spleen extended 4.5 centimeters below the left costal margin and was hard and smooth.

Laboratory findings are as follows:

July 3, 1950		*July 21, 1950*	
Red blood cells	3,400,000	Red blood cells	3,000,000
Hemoglobin	9.2 grams		
White blood cells	98,000	White blood cells	192,000
Granylocytes	80 per cent	Granulocytes	87 per cent
Neutrophiles	42 per cent	Neutrophiles	20 per cent
Segmented	15 per cent	Promyelocytes	1 per cent
Myelocytes	5 per cent	Myelocytes	1 per cent
Metamyelocytes and bands	22 per cent	Metamyelocytes and bands	8 per cent
Eosinophiles	37 per cent	Segmented	10 per cent
Segmented	10 per cent	Eosinophiles	66 per cent
Myelocytes	3 per cent	Bands	3 per cent
Metamyelocytes and bands	24 per cent	Segmented	63 per cent
Basophiles	1 per cent	Basophiles	1 per cent
Metamyelocytes	1 per cent	Lymphocytes	13 per cent
Lymphocytes	20 per cent		
Platelets	158,000	Platelets	Reduced
Slight hypochromia.		Hypochromia, anisocytosis, and poikilocytosis of the erythrocytes.	
16 nucleated erythrocytes per 100 leukocytes.		6 nucleated erythrocytes per 100 leukocytes.	

Bone Marrow Examinations

July 4, 1950		*July 17, 1950*	
L:E ratio	25:1	L:E ratio	10:1
Granulocytes	69 per cent	Granulocytes	81 per cent
Neutrophiles	48 per cent	Neutrophiles	38 per cent
Segmented	7 per cent	Segmented	8 per cent
Bands	10 per cent	Bands	17 per cent
Metamyelocytes	11 per cent	Myelocytes	1 per cent
Myelocytes	19 per cent	Promyelocytes	12 per cent
Myeloblasts	1 per cent		
Eosinophiles	21 per cent	Eosinophiles	41 per cent
Segmented	12 per cent	Promyelocytes	1 per cent

Bands	1 per cent	Myelocytes	8 per cent
Metamyelocytes	7 per cent	Metamyelocytes	2 per cent
Myelocytes	1 per cent	Segmented	20 per cent
		Bands	10 per cent
Lymphocytes	30 per cent	Lymphocytes	10 per cent
Mature	27 per cent	Blasts	4 per cent
Prolymphocytes	4 per cent	Immature	1 per cent
		Adult	10 per cent
		Prolymphocytes	4 per cent
Impression: Probably leukemoid reaction.		Impression: The same as previously.	

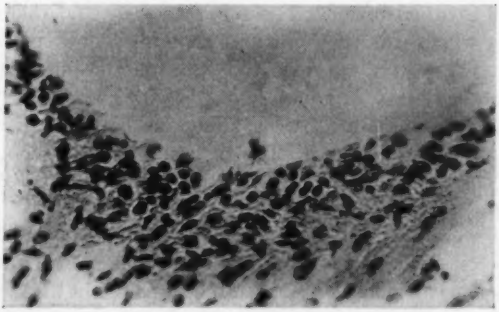

FIG. 1. Eosinophiles infiltrating the wall of a blood vessel.

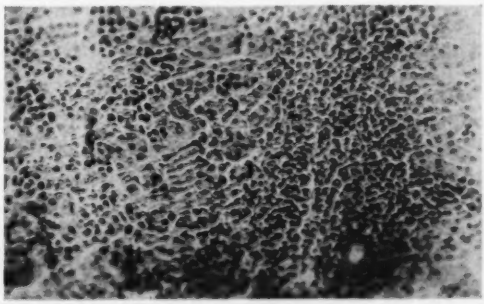

FIG. 2. Eosinophilic infiltration in the liver.

Other Examinations

1. Urinalyses were negative.
2. Pharyngeal cultures were negative for pertussis.
3. Stools for ova and parasites were negative.
4. First and second strength purified protein derivative and trichinella skin tests were negative.

5. X-rays of the chest showed an interstitial diffuse inflammatory process in the inner two-thirds of the right lung.

On July 22, 1950 it was noted that the entire left lung was involved also by this same process. The patient was treated with pertussis human anti-serum, chloromycetin, parenteral fluids, oxygen, and a blood transfusion. The diarrhea and paroxysmal cough improved but the physical findings remained the same. On July 23 the patient passed approximately 75 milliliters of dark, bloody feces and while intravenous fluids were being started death occurred—on the twenty-eighth day of illness.

Post-mortem examination revealed a poorly developed and poorly nourished colored male infant. The lymph nodes were palpable in the cervical, axillary, and inguinal regions. The skin was scaly and there were several firm papules which exuded a creamy, greenish-yellow, purulent material on pressure. There were approximately 20 milliliters of yellow, clear fluid in both pleural cavities. The base of the left lung was loosely adherent to the diaphragm. There were friable adhesions between the visceral and parietal pleura of the left lung. The pleural surfaces of both lungs were roughened. The right and left lungs weighed 49 grams and 46 grams (normal—30 grams).

The lungs were firm and multiple abscess cavities were found in both lungs except for a small area of normal lung tissue in the apex of the left lung. Microscopic examination showed the alveoli to be filled with fibrinous, pink exudate containing numerous eosinophiles, lymphocytes, and fibroblasts.

The liver weighed 238 grams (normal—140 grams) and cut section showed areas of yellow and tan interspaced between brownish-red areas. The spleen was enlarged and firm. The malphigian corpuscles were indistinct. Scattered over the cut surfaces there were numerous dark red areas approximately 0.3 millimeters in diameter surrounded by a dull grey halo.

Microscopically, the general lobular architecture of the liver was overshadowed by leukocytic infiltration. The wall of the central vein was infiltrated with eosinophilic leukocytes. The sinusoids contained eosinophiles and an occasional lymphocyte. The walls of the portal artery and vein were heavily infiltrated with eosinophiles. The lumina of the portal veins were dilated and packed with eosinophiles. The bile ducts were overshadowed by their massive infiltration of leukocytes. The fibrous tissue of the portal canals was heavily infiltrated with leukocytes, chiefly eosinophilic.

The ileum contained about 150 milliliters of dark blood. The colon contained about 100 milliliters of dark, bloody material and the blood vessels over the mucosal surfaces were dilated. No ulcerations or bleeding points could be found.

The lymph nodes in the mediastinum and abdomen varied in size from

0.5 centimeters to 2.0 centimeters and section showed a homogeneous, slightly bulging, red tissue.

Microscopic examination of the heart, spleen, pancreas, gastrointestinal tract, adrenals, lymph nodes, and kidneys showed similar changes as were noted in the liver, that is eosinophilic infiltrations. No fungi were present in cultures of lung abscesses.

This case is believed to be one of leukemoid reaction because of the following:

1. The clinical course.
2. The white blood count above 50,000 per cubic millimeter.
3. The immature normal leukocytes.
4. The presence of leukocytic infiltration in the viscera secondary to an overwhelming pulmonary infection.

DISCUSSION

William A. Howard, M.D.: The term "leukemoid reaction" might more properly be designated as an effect in the infant just described, with the cause of this reaction still not clearly elucidated. This patient died from a profound sepsis with multiple abscesses in the lungs and skin, but a sepsis which was distinguished by the presence of a pronounced hyperleukocytosis in the circulating blood and bone marrow, and a tremendous increase in both the percentage and actual number of eosinophiles in blood and tissue. As a corollary, the final diagnosis in this infant should include some explanation of the eosinophilia.

An increase in eosinophiles is recognized as an important diagnostic sign in many allergic states, intestinal parasitism, amebiasis, and filariasis. If the proportion of eosinophiles is in excess of 20 per cent, trichiniasis or arsenic poisoning may be suspected, while less commonly eosinophilic leukemia, lymphosarcoma or periarteritis may be present. Eosinophilia may occur to its greatest degree, however, as the peculiar response of certain people to chronic infection. Eosinophilia is also a feature of an apparently new clinical entity recently described by Zuelzer and Apt[7]. Characteristics of this group of cases were hyperleukocytosis, eosinophilia of blood and bone marrow, and hyperglobulinemia persisting for long periods in young children ranging in age from eighteen months to three years, and presenting variable clinical pictures. Clinical manifestations described included hematomegaly, splenomegaly, pulmonary infiltrations, asthmatic complaints, joint symptoms, urticaria, and convulsions. Many of the children were symptom-free for much of the course of the disease. Diagnosis of the condition rested on the findings in the liver either by biopsy or at autopsy. The liver lesion consisted of large areas of eosinophilic infiltration with necrosis and granuloma formation, corresponding in general to the

changes described by other authors in the lungs of patients with Loeffler's syndrome. These authors interpreted the findings as the expression of a common pathologic process of variable location and severity, the nature of which is regarded as an allergic tissue response to undetermined antigens. In Zuelzer's cases, all efforts to establish an etiologic agent were unsuccessful. The reported cases, with one exception, were benign and of long duration.

In this infant the course was far from benign, though the duration of illness was somewhat longer than might have been expected from the autopsy findings. Of special significance in this patient were the presence of the generalized skin rash having the appearance of an intrinsic allergic dermatitis (eczema) with secondary furunculosis, and the discovery of multiple lung abscesses. From both of these sources, *Micrococcus pyogenus* variety *aureus* was recovered. In this patient the eosinophilia and leukemoid reaction must certainly be related to an allergic response to infection.

Infectious agents may be antigenic not only from rapid multiplication within the body such as occurs in acute infectious diseases, but also only after remaining in the body for a considerable period, such as occurs in tuberculosis, syphilis, and focal infections. In addition, the "id" reaction is another expression of allergy to bacterial as well as to fungus antigens. Hematogenously borne specific micro-organisms can evoke papular, lichenoid, or bullous lesions as an expression of the antigen-antibody reaction. Here the rash as noted appears to be a secondarily infected eczema complicated by the appearance of metastatic abscesses in the lungs. A less likely possibility is that the rash may be an antigenic response to primary bacterial infection in the lung. In either instance it would appear that the eosinophilia and hyperleukocytosis in this patient are best explained as appearing in the course of an allergic response to infection. The eosinophilic infiltrations into the parenchyma of the various viscera may also, as in Zuelzer's cases, be related in some manner to the pulmonary infiltrations appearing in Loeffler's syndrome.

In spite of the many dissimilar features between this patient and those of Zuelzer and Apt, there remains the possibility that they belong in the same general category, differing only in that the etiologic agent has here been demonstrated. One need not restrict oneself to a single etiologic factor, for if an allergic response is postulated, then any number of antigenic stimuli might be responsible. The specific allergic reaction is dependent, not upon the antigen, but upon the location of the shock tissue.

Our present understanding of eosinophilia as it relates to disease is inadequate. A satisfactory elucidation of the eosinophile must wait upon the study of additional cases such as this.

SUMMARY

1. The literature on leukemoid reactions has been presented.
2. A case of leukemoid reaction in a two month old infant is presented.

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CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: Sanford Leikin, M.D.
Richard J. Waters, M.D.
By Invitation: Benjamin Manchester, M.D.

Sanford Leikin, M. D.

V. R., a four month old colored female was seen in the dispensary with the chief complaint of "chest cold" with noises in the chest.

The patient was apparently well until June 1, 1950 when the mother noticed a severe cough and a considerable amount of whitish "phlegm" in the pharynx of the patient. Associated with this there were loud, rattling noises in the chest. No fever was noted. The patient was seen every other week at the Health Department Clinic and given two shots of penicillin and "cough medicine" without relief. On July 3, the patient was brought to Children's Hospital because the above symptoms had continued.

At that time examination showed a well nourished and well developed colored female with inflamed pharynx, slightly enlarged tonsils, intercostal retraction and coarse rales which cleared on coughing. The apical thrust of the heart was described in normal position and no murmurs were noted. The abdomen was negative and the patient's color was normal. The patient was treated for a pharyngitis with a sulfonamide and neosynephrine nose drops. A PPD #1 was done and also a white blood count and differential (Report under laboratory reports).

The patient returned here two days later. At home she had improved slightly. Physical examination showed improvement of both her pharynx and chest findings. Her temperature was 99.0 F. and her weight was 13 pounds 9½ ounces. Her PPD #1 was negative. PPD #2 was applied; the medicines were continued.

The patient returned two days later, and the symptoms had cleared except that the rattling in the chest remained. Physical examination at this time showed coarse rales throughout the chest "with thick bronchial secretion." The PPD #2 was negative. A chest x-ray was ordered.

On July 10, the patient again appeared in clinic where the findings were the same. The stools were noted to be normal in appearance. Syrup of Calcidine was prescribed at this time.

On July 12, the patient's weight was 13 pounds, 3 ounces and her temperature was 100.4 F. She had been vomiting her medication, and had been febrile since her last visit. Examination of the patient at that time showed the presence of rhonchi and stridor. The heart tones were noted to be poorly heard. The patient was given 300,000 units of crysticillin, and Syrup of Neohetramine was prescribed.

About 2:30 P. M. on July 13 it was noted that the patient was breathing "heavily" and appeared "blue around the lips." She was brought here immediately.

Past history revealed that the patient's mother was sick with a "chest cold" from about the fourth month onward. Two chest plates were done, the reports of which are unknown. The patient was the product of a spontaneous delivery (cephalic presentation), and weighed 7 pounds, 8 ounces at birth. No neonatal difficulties were noted. She was breast fed for the first two weeks and then put on an evaporated milk formula with karo syrup added. She was started on ascorbic acid at two months of age and given cod liver oil, one teaspoonful two times a day. Pureed carrots and applesauce were given in the patient's formula at one month and cereals were offered at three months.

Admission physical examination revealed a well developed, well nourished colored female infant in respiratory distress, breathing with a grunting respiration of about 80 times per minute. She made no movements and the extremities were completely flaccid. Palms, soles, and conjunctivae were pale with a cyanotic tinge. The extremities were cold to touch while the chest was hot and dry. The temperature at this time was 101.6F. The head was symmetrical; the anterior fontanelle was full. There was a profuse growth of hair; the scalp was clean. The eyelids closed and nystagmoid movements of the eyes were noted. Pupils were equal and regular and reacted to light. The tongue was dry and the mucosa pallid. Tonsils were normal. The neck was resistant but no rigidity or masses were noted. There was a groove and flare of the costal cage, and respirations were accompanied by infrasternal indrawing. There was dullness to percussion over the entire left chest and hyperresonance on the right side of the chest with increase in tactile fremitus and breath sounds over this area. There was a decrease in breath sounds over the whole left chest. No rales were heard. These findings in the lungs were noted by one observer. Another observer noted only rough breath sounds. There was dullness over the cardiac area extending to the anterior axillary line. No thrills were palpable and no apex beat was palpable. The heart tones were distant and not clearly made out, but there appeared to be gallop rhythm. The abdomen was soft and flaccid. The liver was palpable about 6 to 7 centimeters below the right costal margin, and the spleen was felt 3 centimeters below the left costal margin. The extremities were cold. All deep tendon and superficial reflexes were absent.

LABORATORY REPORTS

July 3, 1950 Complete blood count.

Leukocytes	11,500 per cubic millimeter
Neutrophiles	31 per cent
Eosinophiles	4 per cent
Basophiles	1 per cent

Lymphocytes..... 62 per cent
Monocytes..... 2 per cent
Platelets—normal. Slight hypochromia of the erythrocytes.

July 7, 1950 X-ray of the chest:

Examination of the chest reveals the bony thorax to be normal. The cardiac silhouette presents an abnormal contour. There is a dense supra-cardiac contour more marked on the left side which involves three-fourth of the width of the chest. Congenital heart should be considered with possible mediastinal effusion. An enlarged thymus cannot be ruled out. The lung fields appear fairly clear.

July 14, 1950 Sickling preparation—negative at the end of 24 hours.

Complete blood count.
Erythrocytes..... 4,300,000 per cubic millimeter
Leukocytes..... 15,800 per cubic millimeter
Lymphocytes..... 92 per cent
Monocytes..... 2 per cent
Neutrophiles, segmented..... 6 per cent
Hemoglobin.....11.8 grams per 100 cubic centimeters.

An electro-cardiogram done just before death revealed: rhythm: nodal, terminating in ectopic beats which coincides with patient's demise. QRS: .08 in lead 1 which becomes abnormally wide in lead 2 with irregular bradycardia.

Lead 1: Moderate Q, high voltage in R wave and deep inverted T.
Lead 2: 5 millimeters, R2 deep wide S2, prominent, T wave, QRS .16
Lead 3: Very few beats, moderate R, wide deep S, prominent upright T.
Interpretation: Gross ventricular arrythmia which coincides with patient's demise.

The patient was immediately put in oxygen. This seemed to help in that she started to cry feebly and move about, but after this she became rapidly worse and died one and one-half hours after being admitted to the ward. It was noted that the patient's heart stopped beating before her respirations ceased.

DISCUSSION

Benjamin Manchester, M.D.: The recognition of cardiac decompensation in an infant is often difficult. It is especially true in this instance because decompensation occurred in a manner that is more often seen in an adult practice. It is rarely seen in children. When failure develops in an infant in the absence of significant cardiac signs, the differential diagnosis must include not only the various types of congenital heart disease, but many of the acquired cardiopathies seen in later life.

The history concerns itself with respiratory distress accompanied by stridor and rhonchi. It was thought to be an acute respiratory infection prior to and during hospitalization. Treatment was ineffective. Enlargement of the liver and spleen and peripheral cyanosis are the significant findings. Tuberculin tests in both strengths were negative. X-ray and electrocardiogram were taken before the infant expired.

In retrospect, it seems probable that the above findings were due to heart disease and decompensation. Of the congenital lesions connected

with stridor and dyspnea, one should consider a right aortic arch associated with anomalous vessels producing a constricting vascular ring. This anomaly may remain "silent." Heart failure is seldom seen with such a defect. Signs of respiratory obstruction are most prominent. Although the chest film was taken in a recumbent position, it showed the heart to be enlarged. The left ventricle is prominent and suggests left ventricular hypertrophy. Such enlargement is not seen in an aortic arch unless associated with an aortic valve deformity.

It is difficult to interpret accurately the great vessel area because of the position in which this film was taken. The widened superior mediastinum may be due to an enlarged thymus or mediastinal nodes, or to some unusual vascular anomaly. The negative tuberculin tests would exclude an acid-fast adenitis. The presence of an enlarged thymus could be confirmed by additional films in the upright position in lateral and oblique views. One may say, however, that the appearance of the widened mediastinal nodes do not resemble that seen with the right aortic arch and anomalous vascular ring.

A single aberrant coronary artery may produce congestive heart failure without warning. Such a vessel may arise from the pulmonary artery or veins and provide an inadequate blood flow. The myocardium is then dependent on the Thebesian circulation.

Sub-aortic stenosis, bicuspid aortic valves or coarctation of the aorta may produce left ventricular hypertrophy and failure. As a rule, such defects can be detected in early life. Palpation of the femoral arteries in an infant in extremis would contribute little toward recognizing coarctation of the aorta.

X-ray showed one additional finding that often is misleading when one considers decompensation. The lungs are clear; there is little evidence of pulmonary engorgement. This would seem, first, to be inconsistent with the suppressed breath sounds and impaired resonance of the left chest noted in the protocol. The electrocardiogram is an agonal one. It contributes little toward a precise diagnosis; it does, however, suggest left ventricular hypertrophy. In lead 1, the high QRS complexes and T wave inversion may be due to left ventricular enlargement or ischemia. If the interpretation is correct, a mechanism producing diminished coronary blood flow must be considered. The aberrant ventricular response and the arrhythmia indicate the critical state of the child.

Another possibility is suggested from the prenatal history. The mother had a "chest cold" from the fourth month until gestation. Endocarditis in utero due to maternal infection is well known. Unhappily, such a possibility is hard to recognize antemortem.

Other congenital lesions such as an intraventricular septal defect, truncus communis, and many cyanotic types of congenital heart disease seem unlikely to have been the cause of heart failure.

It seems most probable that this infant died of congestive heart failure. Whatever the type of heart disease, whether congenital or acquired, there is unmistakable evidence of left ventricular hypertrophy present. It is reasonable to assume that left heart failure had at one time developed. The associated pulmonary engorgement was mistaken for an acute respiratory infection. The cardiac enlargement and the left ventricular hypertrophy produced partial atelectasis or compression of the left lower lobe producing Ewart's sign: dullness, tubular or suppressed breathing, and diminished fremitus of the left lower lobe posteriorly. The continued pulmonary hypertension, as a result of the left ventricular failure, ultimately leads to right heart failure producing venous engorgement and hepato- and spleno-megaly and cyanosis. Peripheral edema is less noticeable in a child or infant that remains in bed. Careful examination of the sacrum and back might have elicited pitting edema.

When right heart failure supervenes secondary to left ventricular decompensation, the stroke-output of the right heart falls. Pulmonary engorgement is reduced. The embarrassed left ventricle is now able to meet the reduced stroke-output of the failing right heart. The dyspnea is then relieved. The x-ray findings will then show a radiolucent lung field. All too often this change is interpreted as evidence of improvement. The present x-ray film shows this quite clearly.

The latter symptomatology is common in adult medicine; it may be as common in infants but my own experience is limited. It is not uncommon to see an adult in acute left ventricular failure: orthopneic, cyanotic, and gasping for breath; sitting on the edge of the bed or in a chair and refusing to lie flat in bed. Only to have such a patient suddenly change for the better. Dyspnea is less; he may be recumbent with ease. The lungs are clear, free of rales. This optimism is usually shattered. On folding back the covers, peripheral edema and an enlarged, sometimes pulsating liver are apparent, indicating the development of right heart failure. Such may be the case here.

PATHOLOGIC DISCUSSION

Richard J. Waters, M.D.
Sanford Leikin, M.D.

At autopsy the body was that of a well developed and well nourished colored female, weighing 5.5 kilograms. On opening the thoracic cavity,

it was noted that the thymus gland was elongated and widened, covering the great veins and the base of the heart.

The heart was markedly enlarged and occupied the entirety of the lower half of the left pleural cavity. It was globular in shape. The heart weighed 87 grams (normal—23 grams). The right atrium and ventricle were dilated, and the left ventricle was hypertrophied. Both systemic and pulmonary venous returns were normal. On opening the heart the most striking feature was the milky-white appearance of the endocardium of the left auricle and ventricle. The endocardium of those chambers was opaque and thickened averaging 2 millimeters. The endomyocardial border was sharply defined but irregular. Some thickening of the mitral valve leaflets was noted. In contrast, the endocardium of the right auricle and ventricle appeared pink, glistening, and transparent. Both coronary arteries arose from behind the cusps of the aortic valve. The intraventricular septum was intact. The foramen ovale and ductus arteriosis were closed. The aorta and pulmonary artery were of normal caliber throughout.

Microscopically, the most signifidant changes were limited to the endocardium of the left auricle and ventricle. The outer portion of the thickened endocardium was composed of parallel-running layers of fibroblasts and loose fibrous tissue. The inner portion was composed of wavy, deeply eosinophilic, elastic fibers. The fibers of the underlying myocardium were thickened and the nuclei were widened. A loss of cross striations was noted. Some myocardial fibers were fragmented while others appeared atrophic with faded nuclei. There were no inflammatory cells in the endocardium or underlying myocardium.

The lungs completely filled the pleural spaces, were light pink, and all lobes were crepitant. The cut surface of the lung was dry and air escaped from the cut alveoli. The liver was enlarged and extended 7 centimenters below the right costal margin. Microscopic sections revealed evidence of early passive vascular congestion. All remaining organs and tissues were normal.

Both grossly and microscopically, the cardiac findings described are consistent with the clinical and pathologic entity, endocardial fibroelastosis.

Dr. Bernice Wedum has reviewed with us both the gross specimen and the microscopic sections of the heart in this case and has stimulated our interest in this entity. We have invited Dr. Wedum to comment on this patient.

Bernice Wedum, M.D.: I am sorry that Dr. Henry Edmonds of the Army Institute of Pathology who showed me the first slides I had ever seen of endocardial fibroelastosis is not here to discuss this case. Regardless of what may be the etiology of the great thickening and change in the char-

acter of the endocardium of the left (and sometimes the right) ventricle, the basic difficulty is obstruction of the Thebesian veins with resulting anoxia of the myocardium. It is a clinical entity at least as definite as Von Gierke's disease and should not be classified as an example of ideopathic hypertrophy.

If one could rely with certainty on the electrocardiogram taken at the point of death and say that evidence suggesting left ventricular hypertrophy was present it would aid greatly in making a diagnosis. I have never had an opportunity to compare such a tracing with one taken prior to death and cannot say how much one can depend on it.

The evaluation of cyanosis in a colored infant, when only 11.8 grams of hemoglobin are present, is difficult since one must have at least 5 grams of reduced hemoglobin in the circulation for visible cyanosis to be present. I believe that one can only say here that cyanosis may or may not have been present prior to its appearance terminally.

In considering the types of heart disease which can cause death in a four month old infant who was apparently well at birth with a clinical picture consisting of questionable cyanosis, a greatly enlarged heart, no murmur, and evidence of both left and right sided heart failure; I would like to add to the limit of possibilities which have been mentioned, transposition of the great vessels without septal defects with a patent ductus arteriosus which had been gradually closing. Absence of heart murmurs and even left axis deviation can occasionally occur in the presence of this malformation. When the enlarged heart was found, one would have been justified in rapidly digitalizing the baby and doing further studies to determine whether this lesion was present since it is amenable to surgery.

A review of the literature reveals one point of interest in the history of children with endocardial fibroelastosis which have been reported and that is the presence of cyanosis in about half the cases in spite of the absence of right to left shunt, diminished blood supply to the lungs, or evidence of changes suggesting arteriosclerosis in the pulmonary vascular bed. Dr. Douglas Cochran of the Department of Pathology of the Johns Hopkins Hospital was kind enough to review a section of the lung in this case and he could find no changes suggesting pulmonary hypertension although he had seen a number of such cases. I would suggest that the cyanosis may be due to decreased cardiac output from a poorly functioning left ventricle resulting in peripheral stasis and excessive oxygen consumption in the tissues. Some sudden episodes of acute cyanosis which occur in these cases may be due to myocardial infarction. I base this suggestion on the fact that Farber has observed areas which resemble healed infarcts in some of these cases although this is far out in the field of speculation.

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